Patent Docket P0897P2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of David V. Goeddel and Mike Rothe Serial No.: 08/446,915 Filed: 22 May 1995 For: Tumor Necrosis Factor Receptor - Associated Factors	Group Art Unit: 1812 Examiner: J. Ulm
	CERTIFICATE OF MAILING I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231 on October 3, 1997 Aida A. Miclat Aida A. Miclat

PETITION TO ACCEPT PHOTOGRAPH AS DRAWING

37 CFR §1.84(b)

BOX ISSUE FEE
Assistant Commissioner of Patents
Washington, D.C. 20231

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OCT 06 1997
GROUP 1800

Sir:

1. Petition is hereby made to accept a photograph in this case.

2. Three (3) copies of the photograph of Figures 1, 2a, 2b, 3, 4, 5, 6a, 6b, 7, 8, 9, 15a, 15b, 16 and 17, are submitted herewith. It is submitted that photographs are the only medium by which to disclose certain aspects of the subject matter sought to be patented in this application.

3. The petition fee under 37 CFR 1.17(h) of $130.00 is to be charged to Deposit Account No. 07-0630. Please charge any deficiency or credit any overpayment to Deposit Account No. 07-0630. A duplicate copy of this sheet is enclosed.

12/02/1997 HPEOPLES 00000026 DAH:070630 08446915
01 FC:122 130.00 CH

Respectfully submitted,
GENENTECH, INC.

Date: October 3, 1997

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Ginger Dreger
Reg. No. 33,055

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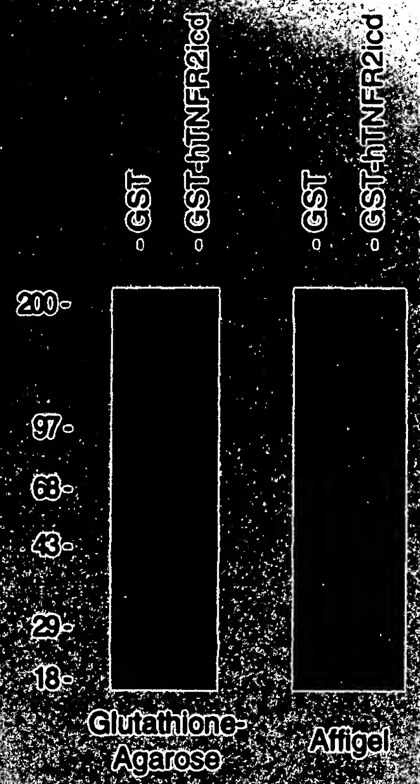
Revised (10/13/95)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GST
GST-hTNFR2icd
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68-
43-
29-
18-
Glutathione-
Agarose
Affigel

FIG. 4

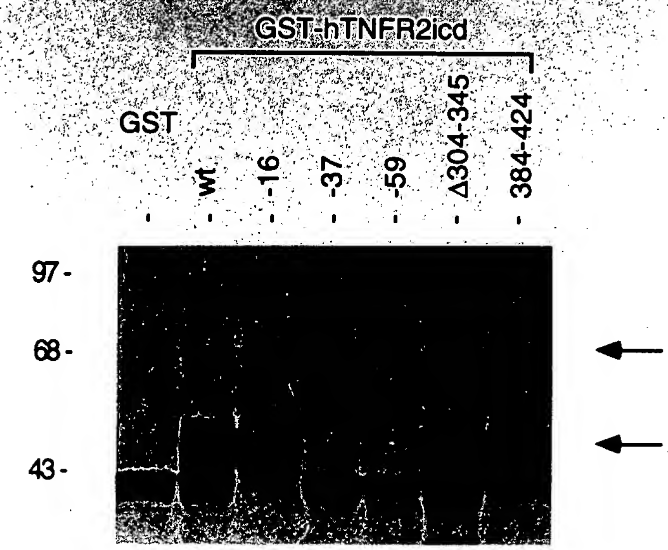
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FIG. 5

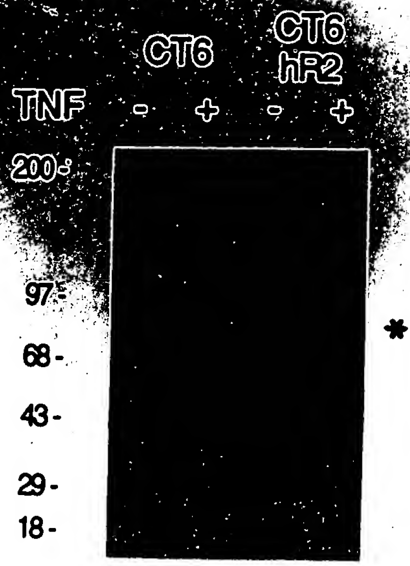
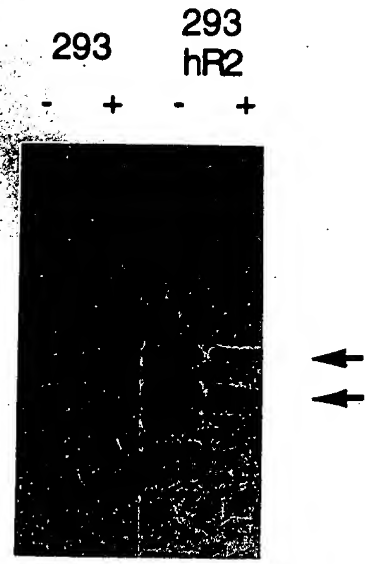


FIG. 2a



CT6

FIG. 2b

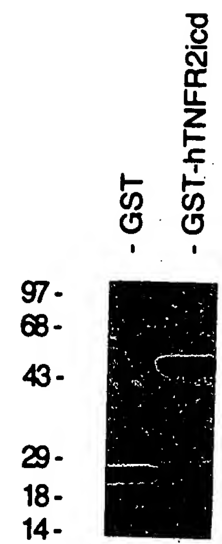


FIG. 3

5741667

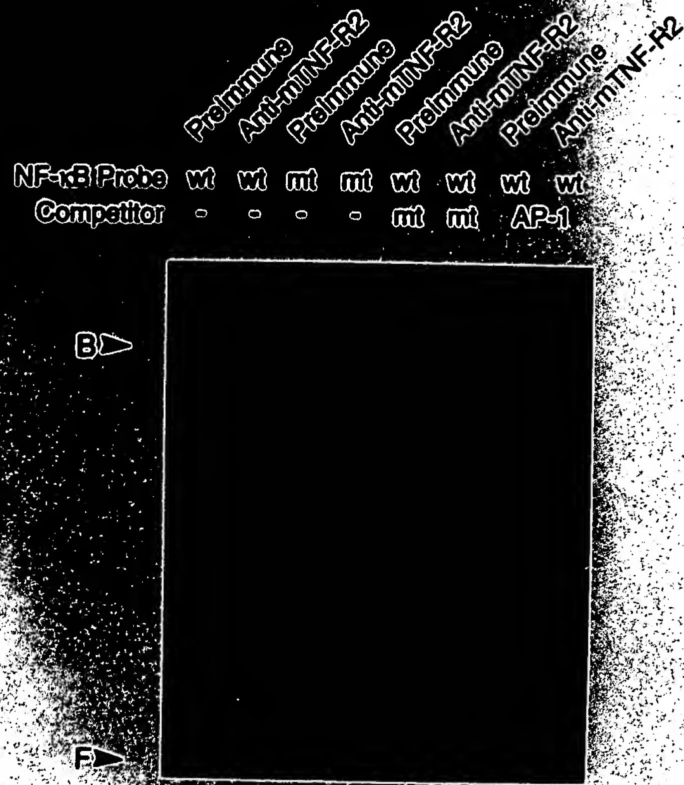


FIG. 1

FIG. 6a

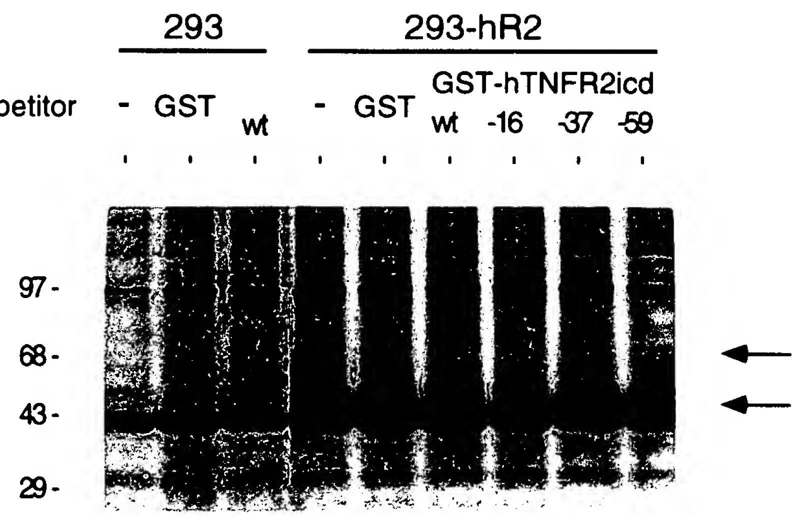


FIG. 6b

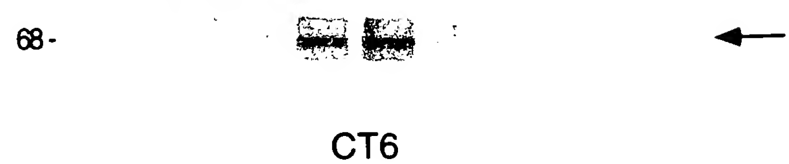
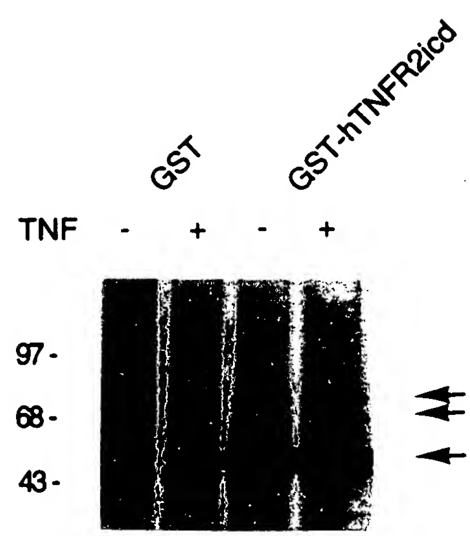
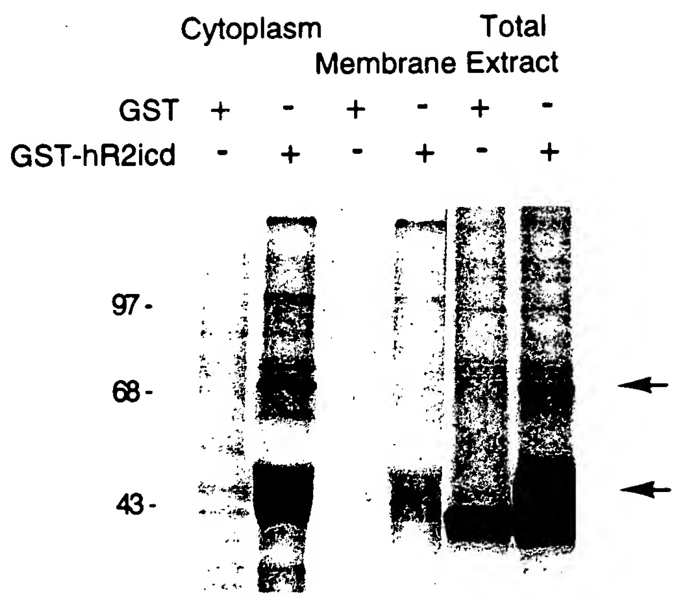


FIG. 7

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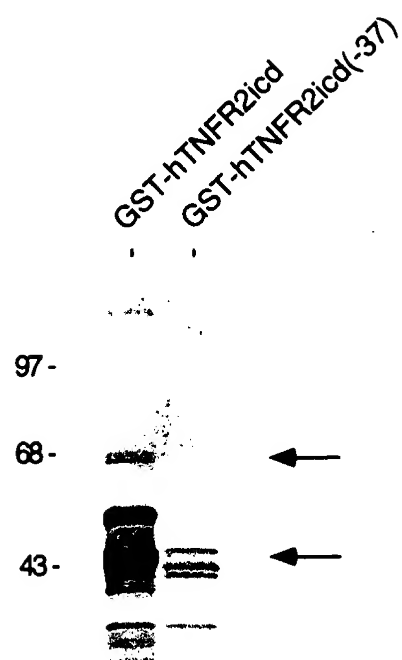
GST-hR2icd - + - + - +
97 -
68 -
43 -

FIG. 8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GST-hTNFR2icd(-37)
97 -
68 -
43 -

FIG. 9

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  1   CCCAGCCCGGTTCTCTGCCCCAAGGACGCTACCGCCCAATGCGAGCAGAAGGCGGCGCACAGATACAGAAAGT
 74  GAGGCTCAGACATATTGAAGACCGTGTGACATAGGGTAGCCAAATGACAGTGTGAGAAAGTGACATTTACTCAAG
149  GCCACCCAGATATCCTGGAGGACCCAGAACCCTGGAGATTCCCATCAGAAAGACCTTCTGGCCACCTGAAACCCC

  1      MetAlaSerSerSerAlaProAspGluAsnGluPheGlnPheGlyCysProProAlaProCysGlnAspPro
224  AAGATGGCCTCCAGCTCAGCCCCTGATGAAAACGAGTTTCAATTTGGTTGCCCCCCTGCTCCCTGCCAGGACCCA

 25  SerGluProArgValLeuCysCysThrAlaCysLeuSerGluAsnLeuArgAspAspGluAspArgIleCysPro
299  TCGGAGCCCAGAGTTCTCTGCTGCACAGCCTGTCTCTCTGAGAACCTGAGAGATGATGAGGATCGGATCTGTCCT

 50  LysCysArgAlaAspAsnLeuHisProValSerProGlySerProLeuThrGlnGluLysValHisSerAspVal
374  AAATGCAGAGCAGACAACCTCCATCCTGTGAGCCCAGGAAGCCCTCTGACTCAGGAGAAGGTTCACTCTGATGTA

 75  AlaGluAlaGluIleMetCysProPheAlaGlyValGlyCysSerPheLysGlySerProGlnSerMetGlnGlu
449  GCTGAGGCTGAAATCATGTGCCCCTTTGCAGGTGTTGGCTGTTCCTTCAAGGGGAGCCCACAATCCATGCAGGAG

100  HisGluAlaThrSerGlnSerSerHisLeuTyrLeuLeuLeuAlaValLeuLysGluTrpLysSerSerProGly
524  CATGAGGCTACCTCCCAGTCCTCCCACCTGTACCTGCTGCTGGCGGTCTTAAAGGAGTGGAAATCCTCACCAGGC

125  SerAsnLeuGlySerAlaProMetAlaLeuGluArgAsnLeuSerGluLeuGlnLeuGlnAlaAlaValGluAla
599  TCCAACCTAGGGTCTGCACCCATGGCACTGGAGCGGAACCTGTCAGAGCTGCAGCTTCAGGCAGCTGTGGAAGCG

150  ThrGlyAspLeuGluValAspCysTyrArgAlaProCysCysGluSerGlnGluGluLeuAlaLeuGlnHisLeu
674  ACAGGGGACCTGGAGGTAGACTGCTACCGGGCACCTTGCTGTGAGAGCCAGGAAGAACTGGCCCTGCAGCACTTG

                        >          +
175  ValLysGluLysLeuLeuAlaGlnLeuGluGluLysLeuArgValPheAlaAsnIleValAlaValLeuAsnLys
749  GTGAAGGAGAAGCTGCTGGCTCAGCTGGAGGAGAAGCTGCGTGTGTTTGCAAACATTGTTGCTGTCCTCAACAAG

200  GluValGluAlaSerHisLeuAlaLeuAlaAlaSerIleHisGlnSerGlnLeuAspArgGluHisLeuLeuSer
824  GAAGTGGAGGCTTCCCACCTGGCACTGGCCGCCTCCATCCACCAGAGCCAGTTGGACCGAGAGCACCTCCTGAGC

225  LeuGluGlnArgValValGluLeuGlnGlnThrLeuAlaGlnLysAspGlnValLeuGlyLysLeuGluHisSer
899  TTGGAGCAGAGGGTGGTGGAATTACAGCAAACCCTGGCTCAAAAAGACCAGGTCCTGGGCAAGCTTGAGCACAGT
```

FIG. 10a

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

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 250 LeuArgLeuMetGluGluAlaSerPheAspGlyThrPheLeuTrpLysIleThrAsnValThrLysArgCysHis
 974 CTGCGACTCATGGAGGAGGCATCCTTTGATGGTACTTTCCTGTGGAAGATCACCAATGTCACCAAGCGGTGCCAC

 275 GluSerValCysGlyArgThrValSerLeuPheSerProAlaPheTyrThrAlaLysTyrGlyTyrLysLeuCys
1049 GAGTCAGTGTGTGGCCGGACTGTCAGCCTCTTCTCTCCAGCTTTCTACACTGCCAAGTATGGTTACAAGTTGTGC

 300 LeuArgLeuTyrLeuAsnGlyAspGlySerGlyLysLysThrHisLeuSerLeuPheIleValIleMetArgGly
1124 CTGCGCTTGTACCTGAACGGGGATGGCTCAGGCAAGAAGACCCACCTGTCCCTCTTCATCGTGATCATGAGAGGA

 325 GluTyrAspAlaLeuLeuProTrpProPheArgAsnLysValThrPheMetLeuLeuAspGlnAsnAsnArgGlu
1199 GAATACGATGCTCTCCTGCCCTGGCCTTTCAGGAACAAGGTCACCTTTATGCTACTTGACCAGAACAACCGAGAG

 350 HisAlaIleAspAlaPheArgProAspLeuSerSerAlaSerPheGlnArgProGlnSerGluThrAsnValAla
1274 CATGCTATTGATGCCTTCCGGCCTGACCTGAGCTCAGCCTCCTTCCAGCGGCCACAGAGTGAGACCAACGTGGCC

 375 SerGlyCysProLeuPhePheProLeuSerLysLeuGlnSerProLysHisAlaTyrValLysAspAspThrMet
1349 AGCGGCTGCCCGCTCTTCTTCCCCCTCAGCAAGCTGCAGTCACCCAAGCACGCCTACGTCAAAGATGACACAATG

                                   <
 400 PheLeuLysCysIleValAspThrSerAla
1424 TTCCTCAAATGCATTGTGGACACTAGTGCTTAGGGATGGGGGGAGGGGGTGTCTCCTGACAGAACCAGCTTAGAC
1499 TGGGGGACTTAGCTAGACAGCCAGGCCCTGCCTGCCCTTGGAGCCCACAGCCCACGACAAGGAGGAGCCAAGGCT
1574 GGCATGACTTCAGCGCCACAGCATGCTGGTTATGGCTGATGTGAGGCTGGAGAAACGTGTGCGTACAGAGACAGA
1649 GTGGAGGAGAAGACAGAAGTGCTCTTTTCACACAGACTACACGACACCAGGAGGCCAGCATGCCAGCAGCTTCTG
1724 AATGTTGAGACCAGCCTAGATCAGGATGAAAAGAGCCAGGCCTGAGGCTTGGACATTGAGCCAAGGCTATGGGGC
1799 CTAAGTGGAGGGGCACTCCTACCAGGACATTCTCTCGAGGTCAGGGCATAACTGGAAAAATGCCCCCATCTCTCT
1874 GTTCAGACTCAAAACTAGAACCACAGGGCAGAAGGGTCAGACATTAATGTGAATTTAACCTGCCCTGGACTGAGT
1949 TCCTATGTTAACAGACACGCAAACAGGTAAACCCAGAAACTGCCCTGGGAAATGCTTTCTGGCTGCATCTGGAGA
2024 TCTTTGATGTTTTTACCGACAAAACAAATAACAAAAGCCTTGAATTGCAAAAAAAAAAAAAAAAA
```

FIG. 10b

```
      ^*  *          *  *
  1                                              MetAlaAlaAlaSerValThrSerPro
  1   GCGCGAAGACCGTTGGGGCTTTGTGGTGTGTGGGGGTTGTAACTCACATGGCTGCAGCCAGTGTGACTTCCCCT

 10 GlySerLeuGluLeuLeuGlnProGlyPheSerLysThrLeuLeuGlyThrArgLeuGluAlaLysTyrLeuCys
 75 GGCTCCCTAGAACTGCTACAGCCTGGCTTCTCCAAGACCCTCCTGGGGACCAGGTTAGAAGCCAAGTACCTCTGT

 35 SerAlaCysLysAsnIleLeuArgArgProPheGlnAlaGlnCysGlyHisArgTyrCysSerPheCysLeuThr
150 TCAGCCTGCAAAAACATCCTGCGGAGGCCTTTCCAGGCCCAGTGTGGGCACCGCTACTGCTCCTTCTGCCTGACC

 60 SerIleLeuSerSerGlyProGlnAsnCysAlaAlaCysValTyrGluGlyLeuTyrGluGluGlyIleSerIle
225 AGCATCCTCAGCTCTGGGCCCCAGAACTGTGCTGCCTGTGTCTATGAAGGCCTGTATGAAGAAGGCATTTCTATT

 85 LeuGluSerSerSerAlaPheProAspAsnAlaAlaArgArgGluValGluSerLeuProAlaValCysProAsn
300 TTAGAGAGTAGTTCGGCCTTTCCAGATAACGCTGCCCGCAGAGAGGTGGAGAGCCTGCCAGCTGTCTGTCCCAAT

110 AspGlyCysThrTrpLysGlyThrLeuLysGluTyrGluSerCysHisGluGlyLeuCysProPheLeuLeuThr
375 GATGGATGCACTTGGAAGGGGACCTTGAAAGAATACGAGAGCTGCCACGAAGGACTTTGCCCATTCCTGCTGACG

135 GluCysProAlaCysLysGlyLeuValArgLeuSerGluLysGluHisHisThrGluGlnGluCysProLysArg
450 GAGTGTCCTGCATGTAAAGGCCTGGTCCGCCTCAGCGAGAAGGAGCACCACACTGAGCAGGAATGCCCCAAAAGG

160 SerLeuSerCysGlnHisCysArgAlaProCysSerHisValAspLeuGluValHisTyrGluValCysProLys
525 AGCCTGAGCTGCCAGCACTGCAGAGCACCCTGTAGCCACGTGGACCTGGAGGTACACTATGAGGTCTGCCCCAAG

185 PheProLeuThrCysAspGlyCysGlyLysLysLysIleProArgGluThrPheGlnAspHisValArgAlaCys
600 TTTCCCTTAACCTGTGATGGCTGTGGCAAGAAGAAGATCCCTCGGGAGACGTTTCAGGACCATGTTAGAGCATGC

210 SerLysCysArgValLeuCysArgPheHisThrValGlyCysSerGluMetValGluThrGluAsnLeuGlnAsp
675 AGCAAATGCCGGGTTCTCTGCAGATTCCACACCGTTGGCTGTTCAGAGATGGTGGAGACTGAGAACCTGCAGGAT

235 HisGluLeuGlnArgLeuArgGluHisLeuAlaLeuLeuLeuSerSerPheLeuGluAlaGlnAlaSerProGly
750 CATGAGCTGCAGCGGCTACGGGAACACCTAGCCCTACTGCTGAGCTCATTCTTGGAGGCCCAAGCCTCTCCAGGA

                                           >         +
260 ThrLeuAsnGlnValGlyProGluLeuLeuGlnArgCysGlnIleLeuGluGlnLysIleAlaThrPheGluAsn
825 ACCTTGAACCAGGTGGGGCCAGAGCTACTCCAGCGGTGCCAGATTTTGGAGCAGAAGATAGCAACCTTTGAGAAC
```

FIG. 11a

```
285  IleValCysValLeuAsnArgGluValGluArgValAlaValThrAlaGluAlaCysSerArgGlnHisArgLeu
900  ATTGTCTGCGTCTTGAACCGTGAAGTAGAGAGGGTAGCAGTGACTGCAGAGGCTTGTAGCCGGCAGCACCGGCTA

310  AspGlnAspLysIleGluAlaLeuSerAsnLysValGlnGlnLeuGluArgSerIleGlyLeuLysAspLeuAla
975  GACCAGGACAAGATTGAGGCCCTGAGTAACAAGGTGCAACAGCTGGAGAGGAGCATCGGCCTCAAGGACCTGGCC

335  MetAlaAspLeuGluGlnLysValSerGluLeuGluValSerThrTyrAspGlyValPheIleTrpLysIleSer
1050 ATGGCTGACCTGGAGCAGAAGGTCTCCGAGTTGGAAGTATCCACCTATGATGGGGTCTTCATCTGGAAGATCTCT

360  AspPheThrArgLysArgGlnGluAlaValAlaGlyArgThrProAlaIlePheSerProAlaPheTyrThrSer
1125 GACTTCACCAGAAAGCGTCAGGAAGCCGTAGCTGGCCGGACACCAGCTATCTTCTCCCCAGCCTTCTACACAAGC

385  ArgTyrGLyTyrLysMetCysLeuArgValTyrLeuAsnGlyAspGlyThrGlyArgGlyThrHisLeuSerLeu
1200 AGATATGGCTACAAGATGTGTCTACGAGTCTACTTGAATGGCGACGGCACTGGGCGGGGAACTCATCTGTCTCTC

410  PhePheValValMetLysGlyProAsnAspAlaLeuLeuGlnTrpProPheAsnGlnLysValThrLeuMetLeu
1275 TTCTTCGTGGTGATGAAAGGCCCCAATGATGCTCTGTTGCAGTGGCCTTTTAATCAGAAGGTAACATTGATGTTG

435  LeuAspHisAsnAsnArgGluHisValIleAspAlaPheArgProAspValThrSerSerSerPheGlnArgPro
1350 CTGGACCATAACAACCGGGAGCATGTGATCGACGCATTCAGGCCCGATGTAACCTCGTCCTCCTTCCAGAGGCCT

460  ValSerAspMetAsnIleAlaSerGlyCysProLeuPheCysProValSerLysMetGluAlaLysAsnSerTyr
1425 GTCAGTGACATGAACATCGCCAGTGGCTGCCCCCTCTTCTGCCCTGTGTCCAAGATGGAGGCCAAGAATTCCTAT

                                                                  <
485  ValArgAspAspAlaIlePheIleLysAlaIleValAspLeuThrGlyLeu
1500 GTGCGGGATGATGCGATCTTCATCAAAGCTATTGTGGACCTAACAGGACTCTAGCCACCCCTGCTAAGAATAGCA
1575 GCTCAGTGAGGAGCTGTCACATTAGGCCAGCCAGGCCCTGCCACACACGGGTGGGCAGGCTTGGTGTAAATGCTG
1650 GGGAGGGCCTCAGCCTAGAGCCAATCACCATCACACAGAAAGGCAGGAAGAAGCCTCCAGTTGGCCTTCAGCTGG
1725 CAAACTGAGTTGGACGGTCCACTGAGCTCAAGGGCCTGGTGGAGCCCGCTGGGGAGCTTCTCAGCTTTCCAATAG
1800 GAAAGCTCCTGCTGTCTCCTCTGTCTGGGGAAGGGAGAGACCTGTAGGTGGGTGCTCAGAAAGGGCCTCTCCAGA
1875 GAGAGTCTCAAGAGCTGCAGCAGGAGCAAAGTGACTGGCCTTCCCCACCCCATCCTTTGGAAAAGAGGTAGCGGC
1950 TACACAGGAGAAGGCATGCGCCTGCAGGGTGTAGCCCAAGAGAGAAGCTCTCTGAGACATAGGCCCTCACTGGAG
2025 AAGGGCCTGCCTGGGCTGCACAGCCTTGCCAGGTGGCCTGTATGGGGGAGAAGTGATTAAATGTTGAGATGTCAC
2100 ACGACAAAAAAAAAAAAAAAA
```

FIG. 11b

FIG. 12a

TRAF2	(mouse)	31	KYLCSACKNILRRPFQA	QCGHRYCSFCLTSI	LSS	GPQNCAACVYE
COP1	(*A. thaliana*)	49	DLLCPICMQIIKDAFLT	ACGHSFCYMCIITH	LRN	KSDCPCCSQH
EFP	(human)	10	ELSCSICLEPFKEPVTT	PCGHNFCGSCLNETWA	VQG	SPYLCPQCRAV
RAD-18	(*S. cerevisiae*)	25	LLRCHICKDFLKVPVLT	PCGHTFCSLCIRTH	LNN	QPNCPLCLFE
UVS-2	(*N. crassa*)	31	AFRCHVCKDFYDSPMLT	SCNHTFCSLCIRRC	LSV	DSK CPLCRAT
RAG-1	(human)	290	SISCQICEHILADPVET	NCKHVFCRVCILRC	LKV	MGSYCPSCRYP
SS-A/Ro	(human)	13	EVTCPICLDPFVEPVSI	ECGHSFCQECISQV	GKG	GGSVCAVCRQR
RING1	(human)	16	ELMCPICLDMLKNTMTTKE	CLHRFCSDCIVTA	LRS	GNKECPTCRKK
RPT-1	(mouse)	12	EVTCPICLELLKEPVSA	DCNHSFCRACITLNYESNRNTDGKGN		CPVCRVP
RFP	(human)	13	ETTCPVCLQYFAEPMML	DCGHNICCACLARCWGTA		ETNVSCPQCRET
c-cbl	(human)	378	FQLCKICAENDKDVKIE	PCGHLMCTSCLTS	WQESEGQ	GSSGCPFCRCE
consensus			---C--C------------ (X11-12)	C-H--C--C---------------- (X10-16)		C--C---

FIG. 12b

TRAF2	(mouse)	157	CPKRSLSCQHC RAPCSHVDLEVHYE VC
		182	PKFPLTCDGCGKKKIPRETFQDHVR AC
DG17	(*D. discoideum*)	171	GGFKLVTCDFCKRDDIKKKELETHYK TC
TFIIIA	(*X. laevis*)	189	QD LAVCDVCNRKFRHKDYLRDHQK TH
XLCOF14	(*X. laevis*)	1	TGKYPFICSECGKSFMDKRYLKIHSN VH
XFIN	(*X. laevis*)	1225	TGEKPYTCTVCGKKFIDRSSVVKHSR TH
ZFY1/2	(mouse)	521	RKKFPHICGECGKGFRHPSALKKHIR VH
MFG2	(mouse)	293	SEEKPFECEECGKKFRTARHLVKHQR IH
RAD18	(*S. cerevisiae*)	183	PNEQMAQCPICQQFYPLKALEKTHLD EC
UVS-2	(*N. crassa*)	182	PDDGLVACPICLTRM KEQQVDRHLDTSC

```
TRAF2    1 MAAASVTSPGSLELLQPGFSKTLLGTRLEAKYLCSACKNILRRPFQAQCG

TRAF2   51 HRYCSFCLTSILSSGPQNCAACVYEGLYEEGISILESSSAFPDNAARREV

TRAF2  101 ESLPAVCPNDGCTWKGTLKEYESCHEGLCPFLLTECPACKGLVRLSEKEH
TRAF1    1 ...............................MASSSAPDENEFQFGCPPA

TRAF2  151 HTEQECPKRSLSCQHCRAPCSHVDLEVHYEVCPKFPLTCDGCGKKKIPRE
TRAF1   20 PCQDPSEPRVLCCTACLSENLRDDEDRICPKCRADNLHPVSPG-SPLTQE

TRAF2  201 TFQDHVRACSKCRVLCRFHTVGCSEMVETENLQDHELQRLREHLALLLSS
TRAF1   69 KVHSDV---AEAEIMCPFAGVGCSFKGSPQSMQEHEATSQSSHLYLLLAV

TRAF2  251 FLEAQASPGTLNQVGPELLQR.............................
TRAF1  116 LKEWKSSPGSNLGSAPMALERNLSELQLQAAVEATGDLEVDCYRAPCCES

TRAF2  272 ..............CQILEQKIATFENIVCVLNREVERVAVTAEACSRQH
TRAF1  166 QEELALQHLVKEKLLAQLEEKLRVFANIVAVLNKEVEASHLALAASIHQS

TRAF2  308 RLDQDKIEALSNKVQQLERSIGLKDLAMADLEQKVSELEVSTYDGVFIWK
TRAF1  216 QLDREHLLSLEQRVVELQQTLAQKDQVLGKLEHSLRLMEEASFDGTFLWK

TRAF2  358 ISDFTRKRQEAVAGRTPAIFSPAFYTSRYGYKMCLRVYLNGDGTGRGTHL
TRAF1  266 ITNVTKRCHESVCGRTVSLFSPAFYTAKYGYKLCLRLYLNGDGSGKKTHL

TRAF2  408 SLFFVVMKGPNDALLQWPFNQKVTLMLLDHNNREHVIDAFRPDVTSSSFQ
TRAF1  316 SLFIVIMRGEYDALLPWPFRNKVTFMLLDQNNREHAIDAFRPDLSSASFQ

TRAF2  458 RPVSDMNIASGCPLFCPVSKME-AKNSYVRDDAIFIKAIVDLTGL
TRAF1  366 RPQSETNVASGCPLFFPLSKLQSPKHAYVKDDTMFLKCIVDTSA
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FIG. 13

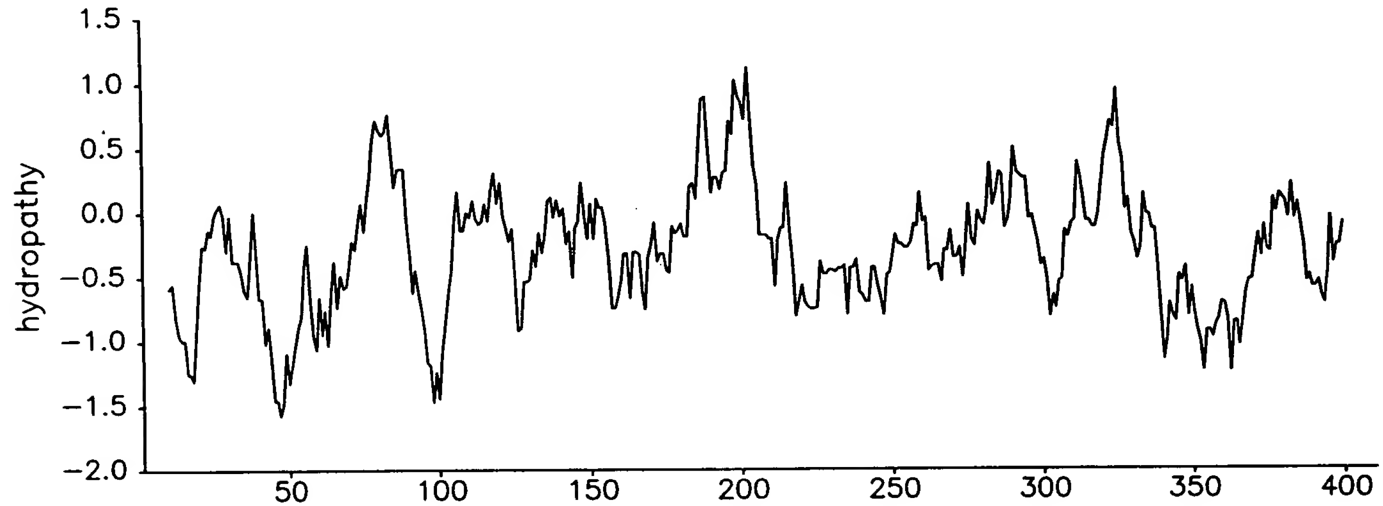


FIG. 14a

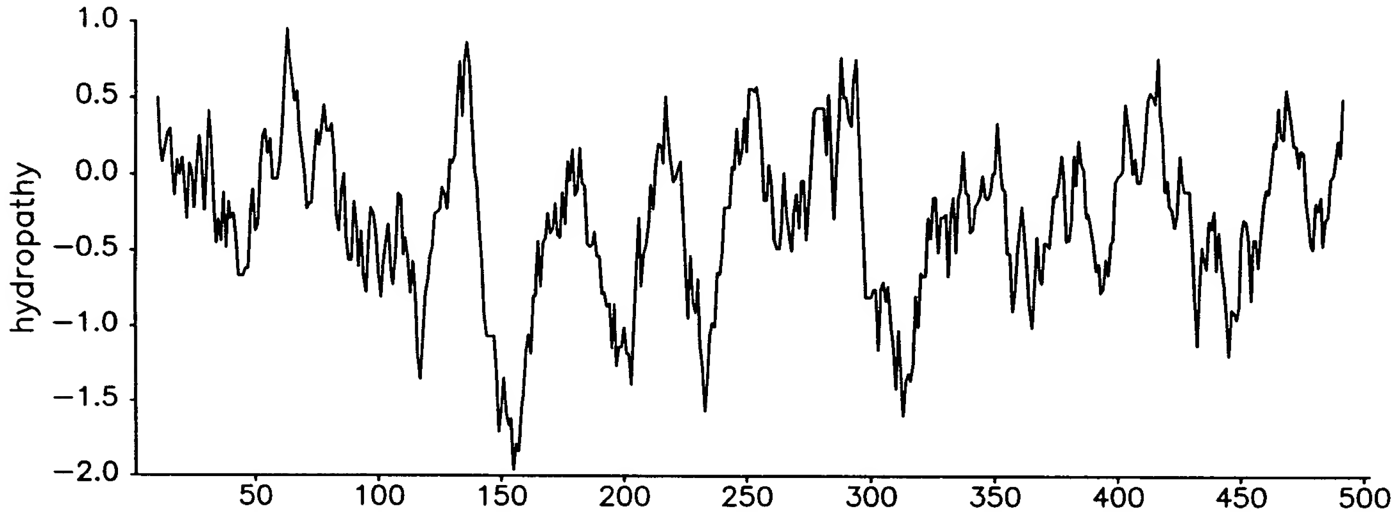

hydropathy
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
50
100
150
200
250
300
350
400
450
500

FIG. 14b

APPROVED BY DRAFTSMAN	O.G. FIG.	
	CLASS	SUBCLASS

FIG. 18a

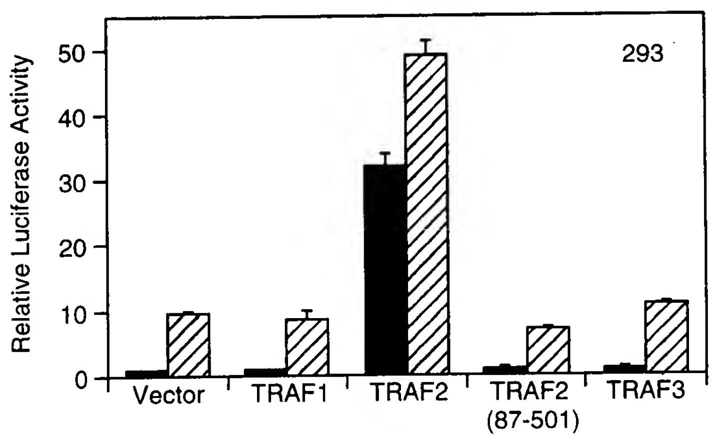


FIG. 18b

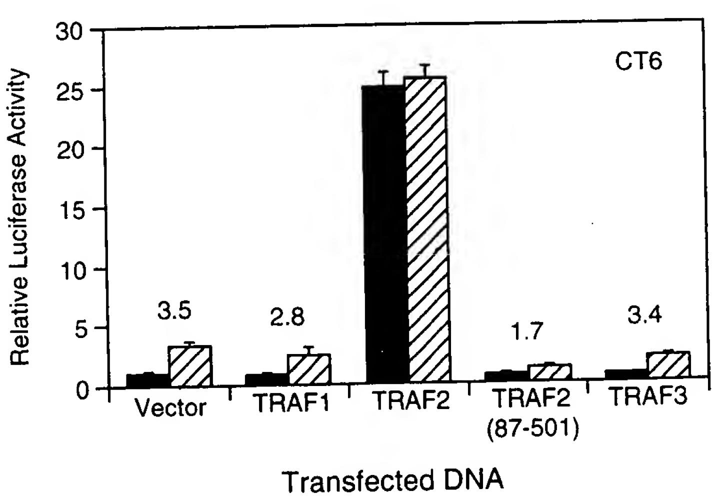


FIG. 19a

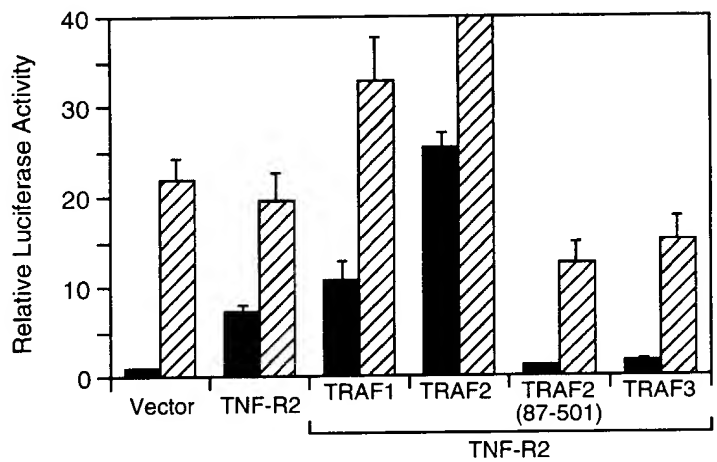
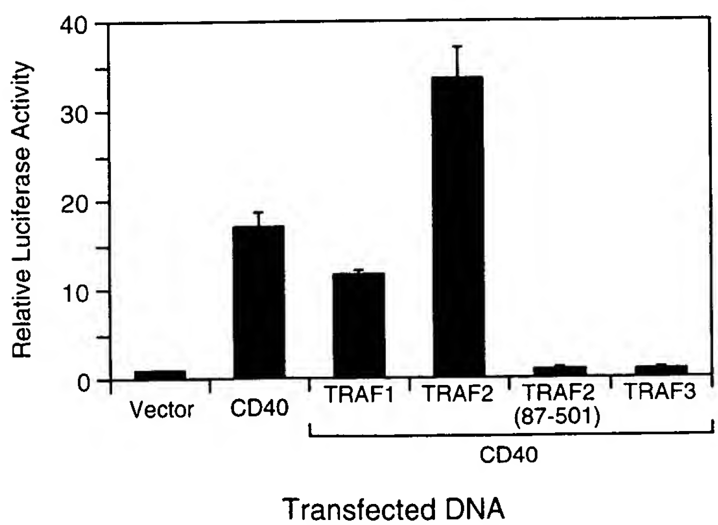


FIG. 19b



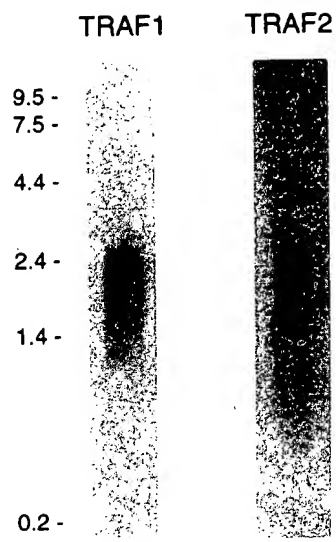


FIG. 15a

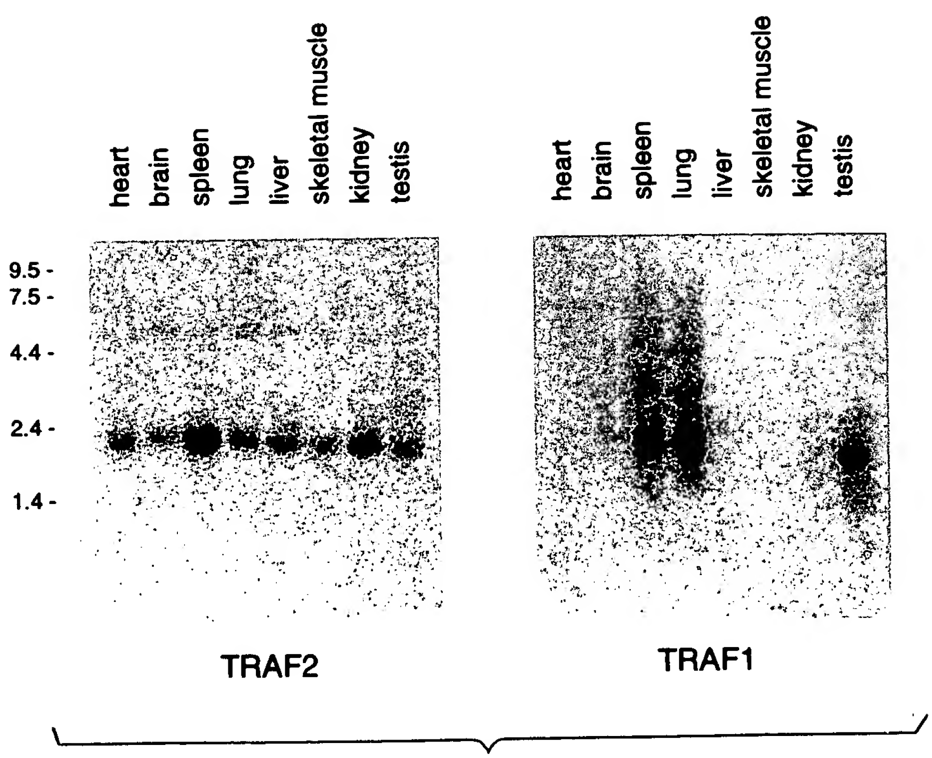


FIG. 15b

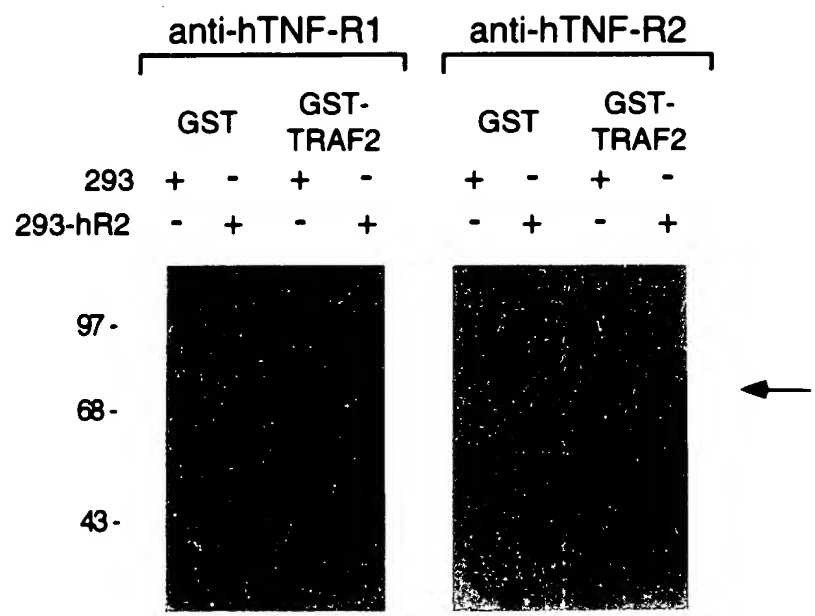
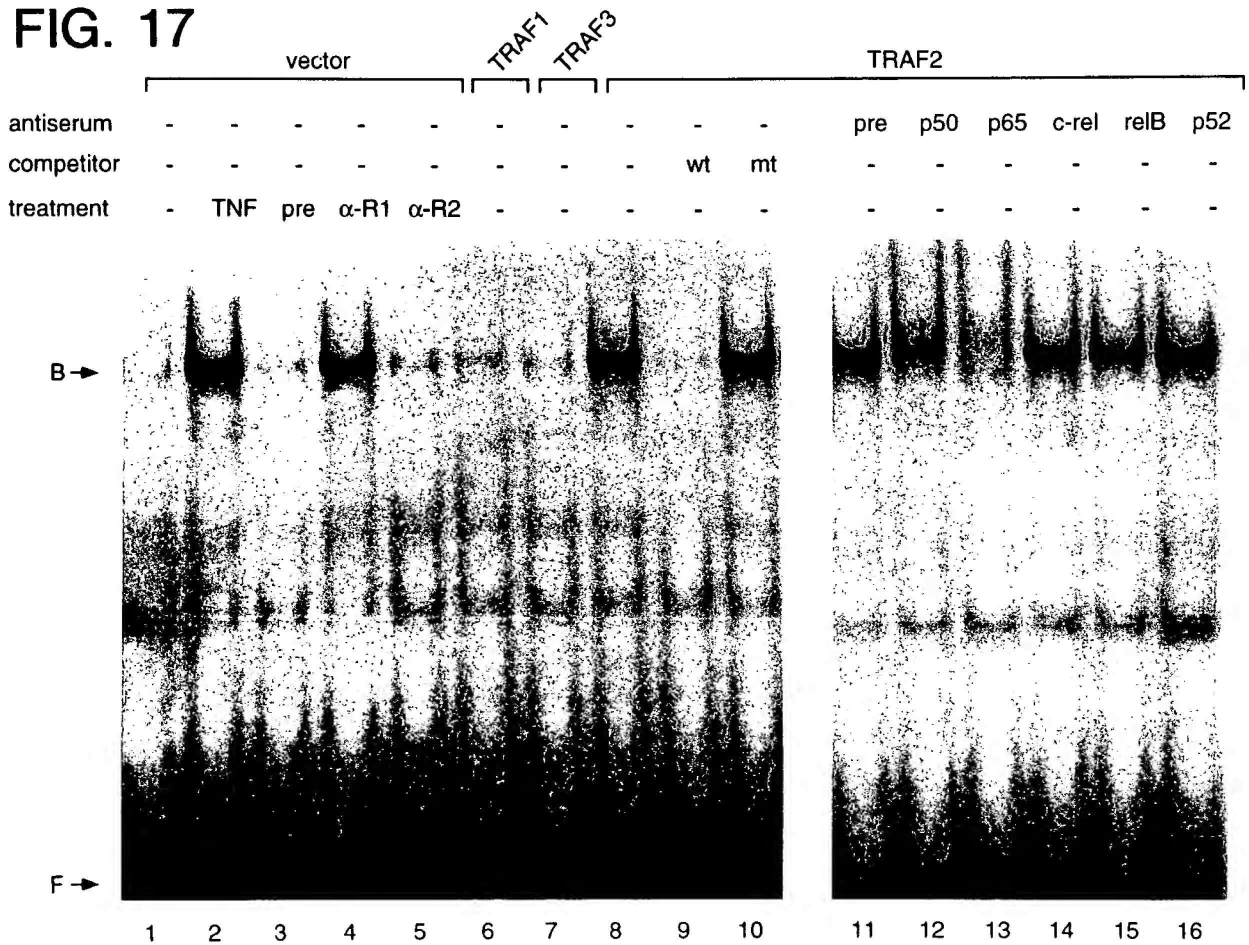

anti-hTNF-R1
anti-hTNF-R2
GST
GST-TRAF2
GST
GST-TRAF2
293 + - + - + - + -
293-hR2 - + - + - + - +
97 -
68 -
43 -

FIG. 16

FIG. 17


vector
TRAF1
TRAF3
TRAF2
antiserum - - - - - - - - - - pre p50 p65 c-rel relB p52
competitor - - - - - - - - wt mt - - - - - -
treatment - TNF pre α-R1 α-R2 - - - - - - - - - - -
B
F
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16